

Acorn NMR, Inc.

NMR Spectroscopy of Codeine

Introduction

A sample identified as Codeine Lot# A-32 was received from Joe Chemist of Company X (100 Main St, Hometown, CA 94551) on 6/14/2010, and assigned Acorn NMR Job # 99999. The work is subject to regulation under GMP. No Method or Protocol was supplied, but confirmation of the structure was requested. The specified solvent was CDCl₃.

Experimental

5.4 mg of Codeine was dissolved in ~0.75 mL of CDCl₃ containing TMS. ¹H, ¹³C, DEPT-135, COSY, HSQC and HMBC spectra were acquired at ambient temperature on a JEOL ECX-400 NMR spectrometer operating at 400 MHz for ¹H and 100 MHz for ¹³C.

The resulting FIDs were transferred to a PC and processed using NUTS NMR processing software from Acorn NMR Inc. ¹H chemical shifts were referenced to TMS, 0 ppm.

Results

The structure was supplied by the submitter with the sample and is shown in Figure 1.

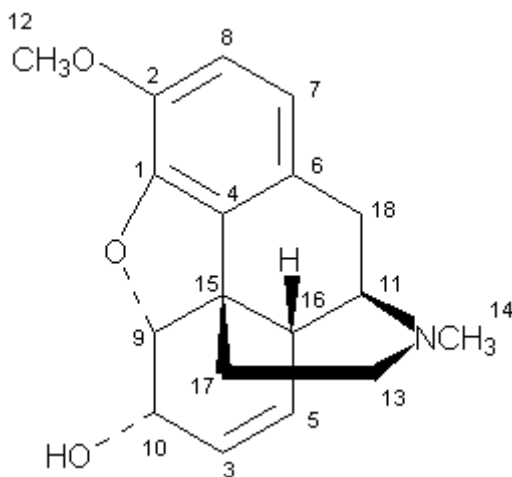


Figure 1

¹H and ¹³C chemical shifts, ¹H multiplicities and observed ¹H-¹H splittings are listed in Table 1. HMBC correlations are listed in Table 2.

Label	¹³ C (ppm)	¹ H (ppm)	Multiplicities*, Splittings (Hz)
1	146.4	-	
2	142.2	-	
3	133.4	5.71	m
4	131.1	-	-
5	128.3	5.29	m
6	127.3	-	-
7	119.6	6.57	d, 8.3
8	113.0	6.66	d, 8.3
9	91.4	4.89	dd, 6.4, 1.3
10	66.4	4.18	br
11	58.9	3.35	br
12	56.4	3.84	s
13	46.5	2.59, 2.40	m
14	43.1	2.44	s
15	43.0	-	-
16	40.8	2.67	br
17	35.8	2.06, 1.88	m
18	20.5	3.04	d, 18.8
"	"	2.30	dd, 18.8, 5.5
OH	-	2.99	br s

* s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad

Table 1

¹ H	¹³ C
3	16
5	10, 11
7	1, 2, 4, 18
8	1, 2, 4 (weak), 6, 7
9	1, 3, 4, 17
11	13, 14 and/or 15, 16
12	2
13	11
14	11, 13
17	13, 15
18	4, 6, 7, 8, 11, 16

Table 2

For any protonated carbon, assignment of either the proton or the carbon can be used to assign the other using the HSQC spectrum. In addition, protonated carbons having odd multiplicity (methyls and methines) may be distinguished from carbons having even multiplicity (methylene) using the DEPT-135 spectrum. Geminal methylene protons are

identified using the HSQC as the two proton peaks with correlations to the same carbon. Quaternary carbons are identified by comparison of the ^{13}C with the DEPT and/or HSQC spectra, as only protonated carbons are observed in either the DEPT or HSQC. Protons on O and N are identified by absence of corresponding peaks in the HSQC spectrum.

H-12 and H-14 were assigned by chemical shift, multiplicity and integration.

C-2 was identified by an HMBC correlation to H-12.

C-1 was assigned based on chemical shift.

H-9 was assigned by chemical shift and an HMBC correlation to C-1. Hs 10, OH, 3, 5, 16, 11 and 18 could then be assigned sequentially from the COSY spectrum.

H-7 and H-8 were identified based on chemical shift, and distinguished by an HMBC correlation between H-7 and C-18.

C-4 was assigned by an HMBC correlation to H-9.

C-6 was assigned by HMBC correlations to H-8 and H-18.

H-13 and H-17 were assigned by chemical shift and COSY correlations, and distinguished by an HMBC correlation between H-13 and C-11.

C-15 was assigned by multiplicity and an HMBC correlation to H-17.

Conclusion

The NMR data are consistent with the proposed structure.

Original spectra will be returned to the submitter with the report.

Per submitter's instructions, the sample will be discarded.

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Reviewed by _____

Abbreviations:

TMS: Tetramethylsilane
DEPT-135: ^{13}C spectrum in which only protonated carbons are observed, and in which the phase of CH_2 peaks is opposite that of CH and CH_3 peaks
COSY: ^1H - ^1H correlation
HSQC: 1-bond C-H correlation.
HMBC: Multiple bond C-H correlation.